**No. 20-1373**

# United States Court of Appeals for the Federal Circuit

BIOGEN INTERNATIONAL GMBH,

*Plaintiff-Appellant*,

v.

BANNER LIFE SCIENCES LLC,

*Defendant-Appellee*.

ON APPEAL FROM THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE
NO. 1:18-CV-02054-LPS (STARK, J.)

## BRIEF OF PHARMACEUTICAL RESEARCH AND MANUFACTURERS OF AMERICA AS *AMICUS CURIAE* IN SUPPORT OF REHEARING *EN BANC* AND REVERSAL

David E. Korn
PHARMACEUTICAL RESEARCH
AND MANUFACTURERS OF AMERICA
950 F Street, NW,
Suite 300
Washington, DC 20004
(202) 835-3400

Kevin F. King
Natalie M. Derzko
Justin W. Burnam
COVINGTON & BURLING LLP
850 Tenth Street, NW
Washington, DC 20001
(202) 662-6000
kking@cov.com

*Counsel for Amicus Curiae*
*Pharmaceutical Research and Manufacturers of America*

May 28, 2020

## CERTIFICATE OF INTEREST

Pursuant to Circuit Rule 47.4, counsel for *Amicus Curiae* Pharmaceutical Research and Manufacturers of America (PhRMA) certifies the following:

1. The full name of every party or *amicus* represented by me in this case is:

   Pharmaceutical Research and Manufacturers of America.

2. The name of the real party in interest represented by me is:

   N/A.

3. Parent corporations and publicly held companies that own 10% or more of stock in the party:

   PhRMA has no parent corporation and no publicly held corporation owns 10% or more of its stock. However, its membership includes companies that have issued stock or debt securities to the public. A list of PhRMA's members is available at: www.phrma.org/about/member-companies.

4. The names of all law firms and the partners or associates that appeared for the party in the lower tribunal or are expected to appear for the party in this Court and who are not already listed on the docket for the current case are:

   Covington & Burling LLP, David E. Korn, Kevin F. King, Natalie M. Derzko, and Justin W. Burnam.

5. The title and number of any case known to counsel to be pending in this or any other court or agency that will directly affect or be directly affected by this court's decision in the pending appeal:

   None.

May 28, 2020

*/s/ Kevin King*
Kevin F. King

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## STATEMENT OF *AMICUS CURIAE*[1]

The Pharmaceutical Research and Manufacturers of America (PhRMA) represents the country's leading innovative biopharmaceutical research companies, which are devoted to discovering and developing medicines that enable patients to live longer, healthier, and more productive lives.[2] Over the past decade, hundreds of new medicines have been approved by the Food and Drug Administration (FDA). Given the risky biopharmaceutical research and development process, which has a significant failure rate, and the substantial requirements to demonstrate safety and efficacy of new products, those results come at a significant cost to PhRMA's members. Since 2000, PhRMA members have invested more than $900 billion in the search for new treatments and cures, including an estimated $79.6 billion in 2018 alone.

PhRMA members depend on a robust system of patent rights. PhRMA aims to advance policies that foster medical innovation, including by ensuring adequate patent protection to enable and provide incentives for its members' substantial in-

[1] Pursuant to Federal Rule of Appellate Procedure 29(a)(4)(E), PhRMA certifies that no party or party's counsel authored this brief in whole or in part, no party or party's counsel contributed money that was intended to fund the preparation or submission of this brief, and no person—other than PhRMA or its members—contributed money that was intended to fund the preparation or submission of this brief.

[2] A complete list of PhRMA members is available at http://www.phrma.org/about/members.

vestments in research and development. To those ends, PhRMA seeks to address barriers that arise from inconsistent legal determinations that undermine intellectual property protections, including through participation as *amicus curiae* before this Court. This case implicates PhRMA's interest in consistent, faithful application of the patent laws because the panel's decision conflicts with Circuit precedent and with the text and purposes of the Hatch-Waxman Act.

## SUMMARY OF ARGUMENT

The *en banc* Court should grant rehearing because the panel's decision is inconsistent with *Pfizer Inc. v. Dr. Reddy's Labs., Ltd.*, 359 F.3d 1361 (Fed. Cir. 2004), and with the Hatch-Waxman Act's text and purposes.

*First*, the panel's decision conflicts with *Pfizer*. Rather than looking to the active moiety of a drug to identify the "product" encompassed by the rights conferred in 35 U.S.C. § 156(b), as this Court did in *Pfizer*, the panel limited those rights to "the approved product." *Pfizer* would have come out differently if the Court had applied the *Biogen* panel's rationale, and that inconsistency affects billions of dollars in investment—making it precisely the sort of important question *en banc* review is designed to address.

*Second*, the panel's decision improperly shifts the Hatch-Waxman Act's balance by permitting generics to circumvent restored patent rights—even when the generic obtains expedited market entry by relying on the innovator's data. Where, as here, the generic company demonstrates the safety and efficacy of its product using the approved innovator product's data, and both the generic and innovator products are claimed by the restored patent and share the same active moiety, the generic infringes the innovator's § 156(b) rights. The statutory text underscores the panel's error, as the term "product" in § 156(b) "includes"—and therefore is not limited to—the "approved product" itself.

*Third*, the panel's decision will hamper innovation by obscuring the extent of restored patent rights for biopharmaceutical companies, which must make substantial investments to research and develop new methods and treatments. That problem is particularly significant for prodrugs—pharmaceuticals that transform (i.e., are metabolized in the body) after administration and represent a sizeable share of biopharmaceutical innovation.

## ARGUMENT

### I. THE PANEL'S DECISION IS INCONSISTENT WITH *PFIZER* AND THE HATCH-WAXMAN ACT'S TEXT AND PURPOSES.

#### A. The Panel's Decision Conflicts with *Pfizer*.

The panel's application of § 156(b) is inconsistent with this Court's statutory interpretation in *Pfizer*. In *Pfizer*, the Court read "product" in § 156(b) to cover the active ingredient, including its salts and esters, and in turn interpreted "active ingredient" to mean the drug's "active moiety." 359 F.3d at 1366 ("'[A]ctive ingredient' as used in the phrase 'active ingredient including any salt or ester of the active ingredient' means active moiety.").

Although the approved drug in *Pfizer* contained amlodipine besylate—a salt of amlodipine, the drug's active moiety—the Court concluded that the active ingredient was amlodipine and thus the "product" for § 156(b) purposes encompassed amlodipine and its salts and esters. *See id.* at 1365-66 ("We conclude that the active ingredient is amlodipine, and that it is the same whether

administered as the besylate salt or the maleate salt."). Thus, even though Dr. Reddy's section 505(b)(2) New Drug Application involved a different amlodipine salt than Pfizer's approved and patented product, the Court held that Dr. Reddy's drug infringed Pfizer's patent-term-restoration rights under § 156(b). Because the statutory text compelled this conclusion, it was irrelevant that the approved product had been "identified … as amlodipine besylate" in FDA records; the active moiety determined the scope of Pfizer's patent-restoration rights. *Id.* at 1365-66.

The panel here parted ways with *Pfizer*. Here, as in *Pfizer*, there is a difference between the active moiety and the administered active ingredient of Biogen's product. Whereas Tecfidera®'s active moiety is monomethyl fumarate (MMF), the active ingredient present at the time of administration is dimethyl fumarate (DMF), an ester of MMF. The body metabolizes DMF into MMF after administration but "before the compound reaches its pharmacological site of action." *Biogen Int'l GmbH v. Banner Life Scis. LLC*, 956 F.3d 1351, 1353-54 (Fed. Cir. 2020). Although the Court held in *Pfizer* that the "product" includes the active moiety in that scenario—such that Biogen's patent-restoration rights would encompass DMF *and* MMF—the panel nonetheless concluded that MMF is not Tecfidera®'s "active ingredient" and therefore is not a "product" within the scope of Biogen's § 156(b) rights. *Id.* The upshot is that this case would have come out differently if the panel had applied *Pfizer*'s statutory interpretation, and likewise *Pfizer* would have

come out differently had the Court applied the reasoning adopted by the panel here. The decisions are irreconcilable.

The panel glossed over this conflict by asserting that *Pfizer* involved "an extension for amlodipine." *Id.* at 1356. But as shown above, the approved drug in *Pfizer* incorporated amlodipine besylate, a salt of amlodipine, rather than amlodipine itself. Once that fact is accounted for, the panel's basis for distinguishing *Pfizer* evaporates—the cases treat similarly situated drugs differently under § 156(b). As the District Court observed, the Court in *Pfizer* rejected "precisely the argument Banner makes here." Appx16.

This Court also explained in *Pfizer* that finding the "therapeutically active agent" amlodipine to be the "active ingredient" (and, therefore, the "product" under § 156(b)) furthered the Hatch-Waxman Act's purposes. 359 F.3d at 1366. Allowing a generic entrant to avoid infringing a restored patent term merely by varying the salt or ester of the active ingredient is a "loophole" that the Act "foresaw" and "guarded against." *Id.*

The panel opened a similar loophole here. It makes no difference that Biogen's drug as administered, rather than Banner's drug, contains an ester of the active moiety. Allowing a generic to avoid infringement by this method defeats § 156(b)'s purpose by providing generics with the benefit of expedited market entry without compensating innovators for their patent term lost to the FDA approval

process. Moreover, the decision discourages development of particular forms of the active moiety that can have beneficial effects on drug properties, including on stability, bioavailability, and pharmacokinetics. Review by the *en banc* Court is warranted to address the inconsistency between the panel's decision and *Pfizer*.

### B. The Panel's Decision Destabilizes the Hatch–Waxman Act's Balance and Contradicts the Act's Text.

Patent term restoration is integral to the Hatch–Waxman Act's dual purposes of facilitating generic entry and providing incentives for biopharmaceutical innovation. As the Supreme Court has explained, the Act was "designed to respond to two unintended distortions" produced by the FDA approval process: the generic's inability to conduct experimental testing during the patent term and the innovator's inability to benefit from its patent rights during the FDA review period. *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661, 669 (1990). The Act addressed the former distortion by allowing generic entrants a safe harbor from infringement for experimental testing and permitting them to rely on data submitted for approval of innovator drugs. It addressed the latter distortion, in part, through the patent-term-restoration provisions of § 156.

The § 156 patent-term-restoration period is an important and tailored incentive for development of new treatments and methods. *See Genetics Inst., LLC v. Novartis Vaccines & Diagnostics, Inc.*, 655 F.3d 1291, 1301 (Fed. Cir. 2011) ("A patent as a whole is extended even though its effect may be limited to certain of its

claims."). This case is about whether Biogen received the full extent of its § 156(b) rights, not about whether Tecfidera® is entitled to those rights in the first place. *See Biogen*, 956 F.3d at 1356 ("This case is not directly governed by *Glaxo*, as it does not involve an issue of a separate extension."). By construing § 156(b) narrowly, the panel's decision creates an incentive for generics to free-ride prematurely on the efforts of innovator companies while depriving innovators of the extended patent term contemplated in the statute.

The panel's decision disrupts the Act's balance. If a generic can seek approval by relying on the data submitted for an innovator drug with the same active moiety, so too should the innovator's rights in the patent-term-restoration period, at a minimum, allow it to exclude the generic's product when used for the same claimed and approved use. *See FDA v. Brown & Williamson Tobacco Corp.*, 529 U.S. 120, 133 (2000) (courts should interpret statutes to "fit, if possible, all parts into an harmonious whole" (citation omitted)); Scalia & Garner, *Reading Law: The Interpretation of Legal Texts* 63 (2012) ("A textually permissible interpretation that furthers rather than obstructs the document's purpose should be favored."). The panel, however, concluded that Banner's generic product does not infringe Biogen's § 156(b) rights, even though Banner's New Drug Application relies on Biogen's data to meet the safety and efficacy requirements for FDA approval. The panel provided no reason why Congress would have designed the Act to work that

way, and none is apparent.

The case for *en banc* review is reinforced by the tension between the panel's decision and the text of § 156. After deciding that the definition of "product" in § 156(f) is limited to "the product as administered and as approved," the panel interpreted the rights conferred by § 156(b) regarding uses of the "product" to mean uses only of the approved product. *See Biogen*, 956 F.3d at 1357. That limiting interpretation contravenes the language of § 156(b), which provides that "[a]s used in this subsection, the term 'product' *includes* an approved product." 35 U.S.C. § 156(b) (emphasis added). By using the word "includes" (rather than "means"), the Act indicates that the definition of "product" is non-exclusive and encompasses a broader set of meanings than merely the approved product. *See Fed. Land Bank of St. Paul v. Bismarck Lumber Co.*, 314 U.S. 95, 100 (1941) ("[T]he term 'including' is not one of all-embracing definition, but connotes simply an illustrative application of the general principle."); Scalia & Garner, *supra*, at 132-33 ("The verb t*o include* introduces examples, not an exhaustive list."); *id.* at 226 (same principle applies in "definitional section[s]"). The panel overlooked this principle and thus bypassed a means of harmonizing its decision with *Pfizer*.

The panel also failed to acknowledge other textual cues that undermine its restrictive interpretation of § 156(b). For example, when the statute refers to a product that has undergone regulatory review, it uses the words "approved prod-

uct." 35 U.S.C. § 156(a) ("The product referred to in paragraphs (4) and (5) [of § 156(a)] is hereinafter in this section referred to as the 'approved product.'").[3] And while the term "approved product" does appear in § 156(b)(3), it is notably absent from § 156(b)(2)—which refers only to a "product." Therefore, the term "a product" under 156(b)(2) does not refer to the same "product" mentioned in 156(a) that leads to entitlement to a patent term extension. There is no reason to limit "product" in § 156(b) to the "approved product" when the statute both (1) expressly states that it uses the term "approved product" to identify the product that has undergone regulatory review and (2) makes clear that "product" merely "includes an approved product."

## II. THE UNCERTAINTY CAUSED BY THE PANEL'S DECISION COULD HINDER INNOVATION AND HAVE A SERIOUS ADVERSE EFFECT IN THE MARKETPLACE.

Patents provide essential economic incentives for the biopharmaceutical industry to take on the substantial costs and risks of developing new medicines and methods. The development of new and improved medicines "typically require[s] significant amounts of pioneering research, and both fixed costs and risks of failing

[3] *See* 35 U.S.C. § 156(a)(4) ("[T]he product has been subject to a regulatory review period before its commercial marketing or use."); *id.* § 156(a)(5)(A) ("[T]he permission for the commercial marketing or use of the product after such regulatory review period is the first permitted commercial marketing or use of the product under the provision of law under which such regulatory review period occurred.").

to develop a marketable product … are very high."[4] "Given the immense investment needed to fund clinical trials on drugs and the ability of generic manufacturers to rely on those tests to secure regulatory approval for their own products, pharmaceutical companies are rarely willing to develop drugs without patent protection."[5] Thus, there is "a causal relationship between the strength of patent rights and innovation."[6]

Patent term restoration is an important component of the Act's carefully balanced incentive structure. Yet the conflict between the panel's ruling and *Pfizer* makes it difficult for biopharmaceutical companies to know in advance how much protection their products will receive. That uncertainty regarding the extent of § 156(b) rights could hamstring pharmaceutical innovation. *En banc* review is needed to clarify the rights provided for innovator drugs during the restoration period.

Such clarity is particularly important for companies developing prodrugs—that is, drugs administered in one form that are converted in the body to another

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[4] Fed. Trade Comm'n, *To Promote Innovation: The Proper Balance of Competition and Patent Law and Policy*, ch. 3, at 5 (Oct. 2003), https://www.ftc.gov/sites/default/files/documents/reports/promote-innovation-proper-balance-competition-and-patent-law-and-policy/innovationrpt.pdf.

[5] Benjamin N. Roin, *Unpatentable Drugs and the Standards of Patentability*, 87 Tex. L. Rev. 503, 503 (2009).

[6] Stephen Haber, *Patents and the Wealth of Nations*, 23 Geo. Mason L. Rev. 811, 829 (2016).

form with therapeutic activity. Prodrugs account for a sizeable share of innovation in the biopharmaceutical sector and provide treatments for a wide range of conditions.[7] Yet because these drugs are designed for post-administration transformation within the body, the panel's ruling—which limits § 156 restoration rights to a drug's active ingredient "when administered," *Biogen*, 956 F.3d at 1356 (citation omitted)—signals that a patentee's § 156(b) rights may offer more limited protection against generic versions. This potential adverse effect on prodrug development reinforces the need for *en banc* review.

* * *

The scope of a patent holder's rights under § 156(b) affects billions of dollars in investments and goes to the heart of the balance struck in the Hatch-Waxman Act. *En banc* review is warranted given the "exceptional importance" of these issues to the industry and the need to "maintain uniformity of the court's decisions." Fed. R. App. P. 35(a)(1)-(2).

[7] *See* J. Rautio et al., *Prodrugs—Recent Approvals and a Glimpse of the Pipeline*, 109 Eur. J. Pharm. Sci. 146, 146 (2017) (prodrugs "accounted for about 10% of all [approved] small molecular weight drugs" over five-year period).

## CONCLUSION

The rehearing petition should be granted.

Respectfully submitted,

*/s/ Kevin King*

David E. Korn
PHARMACEUTICAL RESEARCH
AND MANUFACTURERS OF AMERICA
950 F Street, NW,
Suite 300
Washington, DC 20004
(202) 835-3400

Kevin F. King
Natalie M. Derzko
Justin W. Burnam
COVINGTON & BURLING LLP
850 Tenth Street, NW
Washington, DC 20001
(202) 662-6000
kking@cov.com

*Counsel for Amicus Curiae Pharmaceutical Research and Manufacturers of America*

May 28, 2020

## CERTIFICATE OF COMPLIANCE

Pursuant to Federal Rules of Appellate Procedure 29 and 32 and Federal Circuit Rule 35, I certify the following:

1. This brief complies with the type-volume limitations of Federal Circuit Rule 35(g) because it contains 2,598 words, excluding the parts of the brief exempted by Federal of Appellate Procedure 32(f).

2. This brief complies with the typeface requirements of Federal Rule of Appellate Procedure 32(a)(5) and the type-style requirements of Federal Rule of Appellate Procedure 32(a)(6) because it has been prepared using Microsoft Word Professional Plus 2016 in 14-point Times New Roman font.

May 28, 2020

*/s/ Kevin King*
Kevin F. King
*Counsel for Amicus Curiae*

## CERTIFICATE OF SERVICE

I hereby certify that on May 28, 2020, I caused the foregoing brief to be filed with the Clerk of the U.S. Court of Appeals for the Federal Circuit using the CM/ECF system and to be served upon counsel for all parties via the CM/ECF system.

*/s/ Kevin King*
Kevin F. King
*Counsel for Amicus Curiae*